UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,684	07/17/2003	Scott A. Waldman	TJU0001-107	1770

35148 7590 05/16/2007

Pepper Hamilton LLP
500 Grant Street
One Mellon Bank Center, 50th Floor
Pittsburgh, PA 15219-2502

EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
05/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,684	WALDMAN, SCOTT A.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25-27,30-34,36,38-48 and 50-61* is/are pending in the application.

4a) Of the above claim(s) *59-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23, 25-27, 30-34, 36, 38-48 and 50-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

JON EPPERSON
PRIMARY EXAMINER

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/28/06;4/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-22, 24, 28, 29, 35, 37, and 49 have been cancelled as filed 2/27/07.

Claims 57-61 have been added as filed 2/27/07.

Claims 23, 25-27, 30-34, 36, 38-48 and 50-61 are currently pending.

Claims 59-61 have been withdrawn.

Claims 23, 25-27, 30-34, 36, 38-48 and 50-58 are being examined in this application.

Election/Restrictions

2. Applicant's election without traverse of Group I (new claims 23-44), and species election of peptide having amino acid sequence of SEQ ID NO: 2 as the ST receptor binding ligand, and 5-fluorouracil as the species of active agent, in the reply entered, 02/01/05, is as previously acknowledged.

Applicants' response to the restriction requirement addresses that the instant claim composition includes both conjugated and unconjugated compositions. Applicant's response has been considered and the instant claim pharmaceutical compositions are considered to include both conjugated and unconjugated compositions. No restriction between the conjugated or unconjugated compositions has been made, as previously acknowledged.

The added Claims 45-47 (as filed on 11/2/05), Claims 48-56 (as filed on 8/2/06), and Claims 57-58 (as filed on 2/27/07) are grouped together with the elected Group I, and are examined as one group of invention.

3. Newly submitted claims 59-61 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims 59-61 are drawn to a method of treating an individual comprising various steps and/or reagents, and the invention originally elected (Group I) is drawn to a pharmaceutical composition. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, Group I invention is drawn to a pharmaceutical composition comprising various reagents, which can be used in different processes such as for immunoassay for detecting ST receptor, or for screening other binding proteins. Thus, the inventions are distinct.

In addition, applicants state "new claims 59-61 which read on non-elected Group V". (Reply, p. 11, para 2).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 59-61 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

2. This application is a continuation of 09/263,477 (now abandoned), filed 3/5/99, which is a continuation of 08/583,447 (now US Patent 5,879,656), filed 1/5/96, which is a continuation-in-part of 08/141,892 (now US Patent 5,518,888), filed 10/26/93.

However, the Grandparent patent application 08/141,892 (Now US Patent 5,270,964) do not appear to provide supports for the claimed invention regarding SEQ ID NO: 55 and 56, which are recited in Claims 25, 32, 43, 45, and 50 of the instant application.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Thus, the instant claims 25, 32, 43, 45, and 50 which recite sequences not disclosed in the parent applications are entitled only to the filing date of the application 08/583,447.

The filing date of the instant claimed invention of recited in Claims 25, 32, 43, 45, and 50 (in particular, SEQ ID Nos 55 and 56) is determined as the filing date of the US Application 08/583,447, **01/05/1996**.

Information Disclosure Statement

3. The references cited in the Information Disclosure Statement filed on 9/28/06 has been fully considered. See the attached PTO 1449.

The information disclosure statement filed 4/27/07 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that

portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Applicants state the copies of the references cited in the 4/27/07 IDS can be found in earlier filed applications. However, the copies for the references (cited in 4/27/07 IDS) are not found in the following earlier filed applications: 09/263,477; 08/583,447; 08/141,892.

Applicants are respectively directed to 37 CFR 1.98 (d):

"(d) A copy of any patent, publication, pending U.S. application or other information, as specified in paragraph (a) of this section, listed in an information disclosure statement is required to be provided, even if the patent, publication, pending U.S. application or other information was previously submitted to, or cited by, the Office in an earlier application, unless:

(1) The earlier application is properly identified in the information disclosure statement **and** is relied on for an earlier effective filing date under 35 U.S.C. 120; and

(2) The information disclosure statement submitted in the earlier application complies with paragraphs (a) through (c) of this section."

(emphasis added).

Specification

4. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the **abstract not exceed 150 words** in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Applicants are also invited to update the continuing data (benefits claimed under 35 USC 119, 120, etc.) in the first line of the specification.

Claim Rejections Withdrawn

5. In light of applicants' amendments to the claims and supporting arguments, the following claim rejections as set forth in the previous office action are withdrawn:

A.) Claims 28, 30-34, 36, and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection over Claim 28 is moot due to applicant's cancellation of the claim.

B.) Claims 23 and 28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 6, and 8 of U.S. Patent No. 6,060,037 (Claims 5 and 1 of the '220 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claims the same pharmaceutical compositions as the instant application.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

7. Claims 23, 25-27, 30-34, 36, 38-48, and 50-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record as set forth in the Office action, mailed 9/6/06, at pp. 8+. The rejection over claims 28 and 49 is moot due to applicant's cancellation of the said claims. The rejection over claims 57 and 58 is necessitated by applicant's amendment to the claims. Due to applicants' amendments to the claims, the rejection is rewritten below.

The instant claims recite a product of pharmaceutical composition comprising: a) ST receptor binding ligand selected from the group consisting of: antibodies that bind to ST receptor, antibody fragments that bind to ST receptor and peptides that bind to ST receptor; b) a non-peptide radiostable therapeutic agent; and, c) a pharmaceutical carrier or diluent.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to the decision of The Court of Appeals for the Federal Circuit, which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a

precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

Claims 23, 42, and 48 are drawn to a genus of "pharmaceutical compositions" comprising a genus of ST receptor binding ligand, and a genus of active (or therapeutic) agent. The instant claims (e.g. claim 25) are also drawn to a genus of peptide sequences recited in 50+ different sequences. The instant claims recite (e.g. Claim 25) "peptides having **an** amino acid sequence SEQ ID NO:2 ..." and "fragments and derivatives of such peptides" (emphasis added). Thus, the claims can be interpreted to mean any "fragment" of the recited SEQ ID No. The term "an" amino acid sequence can be broadly interpreted to mean any fragments within the sequence dictated by the recited SEQ ID Nos.

Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "pharmaceutical compositions" comprising various ST receptor ligands, active agents, and/or "peptides" (or fragments thereof) that are capable of binding to ST receptors. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of "pharmaceutical composition" for using to treat various diseases. That is the claimed "pharmaceutical composition" can comprise

any ST receptor binding ligand (i.e. any peptide, any antibody, and fragments thereof) and any active agent that can be any molecules.

The instant specification defines the term "ST receptor" as "refer to the receptors found on colorectal cells, including local and metastasized colorectal cancer cells, which bind to ST" (emphasis added; p. 6, lines 13+). This functional definition for the "ST receptor" is broad and encompasses any entities that "bind to ST". The instant specification also broadly defines the term "ST" as "refer to heat-stable toxin (ST) which is a peptide produced by *E. coli*, as well as other organisms" (p. 6, lines 6+), which encompasses any peptide that is "heat stable" and produced by any organism. The instant specification does not provide common core structure for "ST". The instant disclosure also does not provide common core structure for the "receptors" that would bind to a "ST".

Since the definition for the term "ST receptor" depends on the scope and structure of the term "ST" as described in the instant disclosure, the possession of the "ST receptor" cannot be demonstrate without demonstrating the possession of "ST" peptides. As stated above, the instant specification does not provide common core structure or representative number of species for the claimed "ST" peptides to demonstrate possession of the entire genus of "ST". Thus, the instant specification does not demonstrate the possession of the entire claimed genus of "ST receptor".

"A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. See also Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991))."

(MPEP 2163; emphasis added)

As discussed above, the definitions for the terms "ST receptor" or "ST" are "by function" (i.e. binding to ST; or binding to ST receptor). These functional limitations only provides what the "ST" or "ST receptor" does, "rather than what it is".

In addition, the instant specification also does not demonstrate possession of the entire claimed genus of "pharmaceutical composition", which term broadly reads on using the composition for various treatments in animals and/or human. The only examples of "pharmaceutical composition" are the conjugates used to inhibit T84 cells in vitro in the instant specification at p. 72-75 (especially Example 6). The instant specification does not disclose any pharmaceutical composition other than the conjugates used to inhibit the T84 cells. No example of "pharmaceutical composition" that can be used to treat human and/or animals for various diseases is described in either the instant specification or claims. That is the instant specification does not adequately describe compositions that can be used for pharmaceutical purposes including administering to humans and/or animals of the claimed peptide-agent conjugates.

In addition, the instant claims also drawn to a genus of peptides and/or antibody fragments, as discussed above. The term "fragments" is broad and encompasses fragments comprises almost any numbers of amino acids. For example, a fragment can be a peptide comprising two amino acids, which when formulated to be a part of the pharmaceutical composition may or may not exhibit the desired pharmaceutical effects. The instant specification also does not provide representative number of species of the claimed "fragments" of the "ST receptor binding ligands", antibodies, or peptides (or fragments thereof) of the SEQ ID Nos that are capable of binding to the "ST receptor".

"Noelle v. Lederman, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described)."
(see MPEP 2163 II).

As discussed above, the instant specification does not demonstrate the possession of the entire claimed genus of "ST receptor" (i.e. "the antigen"). Thus, the possession of the claimed genus of "antibodies" and fragments thereof is also not demonstrated.

Therefore, applicants are not in possession of the claimed genus of "pharmaceutical composition" that comprises any ST receptor ligands, active agents, and/or peptide fragments. Applicant's claimed scope represents only an invitation to experiment regarding possible compositions that might be generated and used for pharmaceutical purposes.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the amended claims now recite "the ST receptor ligand is selected from the group of antibodies that bind to ST receptor, antibody fragments ... that bind to ST receptor" and "bind to ST receptor", and thus the instant specification demonstrates possession of the

claimed genus of "ST receptor ligands". (Reply, p. 12, para 2). Applicants also argue assert that the term "fragments" has been further limited by referring to its "function of binding to ST receptor". (Reply, p. 13, para 2).

Contrary to applications assertion, the mere reciting of the general terms such as "antibodies", "antibody fragments", or "peptides", do not provide evidence to demonstrate possession of the claimed genus of compounds such as the genus of "ST receptor ligands". Besides the recited common function of "binding ST receptor", applicants have not provided any evidence or specific disclosure from the instant specification to indicate common core structure of the claimed genus of "ST receptor ligands".

"A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. See also Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991))."
(MPEP 2163; emphasis added)

As discussed above in the body of the rejection, the definitions for the terms "ST receptor" or "ST" are "by function" (i.e. binding to ST; or binding to ST receptor). These functional limitations only provides what the "ST" or "ST receptor" does, "rather than what it is".

Thus, the instant specification has not demonstrated possession of the entire claimed genus of "ST receptor ligand" and/or "ST receptor".

"Noelle v. Lederman, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described)."
(see MPEP 2163 II).

As discussed above, the instant specification does not demonstrate the possession of the entire claimed genus of "ST receptor" (i.e. "the antigen"). Thus, the possession of the claimed genus of "antibodies" and fragments thereof is also not demonstrated.

Applicants also argue "the specification is replete with specific examples of the claimed invention"(i.e. pharmaceutical composition), and provides "Example 1" of the instant specification as examples. (Reply, p. 13, para 1).

The term "pharmaceutical composition" is broadly interpreted to mean compositions that can be administered to animals and humans to elicit pharmaceutical effects (such as therapeutic treatments for certain diseases). As discussed above, the instant specification does not provide representative number of species to indicate possession of such compositions.

In Example 1 of the instant specification only provided a list of compounds without providing specific examples of administering the listed compounds to animals or humans for various pharmaceutical effects.

Merely providing a "laundry list" of species do not convey possession of the entire genus (i.e. the genus of "pharmaceutical composition"). See MPEP 2163 I:

"A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967)"
(emphasis added).

Scope of Enablement Rejection

9. Claims 23, 25-27, 30-34, 36, 38-48, and 50-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for use in isolated cells, does not reasonably provide enablement for pharmaceutical uses in animals or humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record as set forth in the Office action, mailed 9/6/06, at pp. 8+. The rejection over claims 28 and 49 is moot due to applicant's cancellation of the said claims. The rejection over claims 57 and 58 is necessitated by applicant's amendment to the claims.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants notes "the claim does not contain any reference or limitation with respect to intended use". (Reply, p. 14, para 1).

The instant claims recite "a pharmaceutical composition", which is intended to be used for treatments of certain diseases. In accordance with 35 USC 112 1st paragraph, the specification should "enable" "any person of skilled in the art" to "make and use" the claimed invention. Thus, to satisfy the "enablement" requirement, the pharmaceutical uses of the entire claimed genus of "pharmaceutical compositions" need to be demonstrated.

Applicants state that "the application contains no in vivo data but does include numerous examples of embodiments and extensive discussion of how to make and use the invention." (Reply, p. 14, para 3).

Applicant's above statements provide further indication that the instant specification does not provide guidance to enable one skilled in the art to make and use the claimed invention. As discussed above, "pharmaceutical composition" requires administering the claimed "composition" to human and/or animals and to elicit certain pharmaceutical effects in said human and/or animals. That is "in vivo" (i.e. usage in human and/or animal) data would be required to demonstrate the use of the entire scope of the claimed invention.

As discussed in the previous rejection and as pointed out by the applicants, the instant specification only provides examples of using the claimed invention in cells, but not in whole animals and/or human. There is also no evidence to indicate that usage of the claimed composition in cells can be "reasonably correlated" to the entire scope of the claimed invention (i.e. utility in human and animals). See MPEP 2164.01(c).

Thus, applicants have not demonstrate the entire scope of the claimed invention is enabled.

Applicants also argue "none of the references cited by the Office raise any specific issues of non-enablement". (Reply, p. 15, para 3).

Contrary to applicants' assertion, the previously cited references provide ample evidence to demonstrate the "unpredictability" of using peptide or protein as pharmaceutical compositions. Applicants seem to argue that because some of the peptide drugs taught by the references (e.g.

Cianfrocca et al) have limited effectiveness, peptide drugs, in general, are predictable and can be used as drugs. Although certain peptides (such as some of the peptides) taught by Cianfrocca reference have limited success, using peptides as drugs in general are highly unpredictable.

Applicants also state "nothing in the reference supports the conclusions that peptides cannot be used as drugs" (Reply, p. 14, para 5), which statement seems to imply that the previous rejection was over the total non-enablement of the peptide drug. However, the previous rejection is a "scope of enablement rejection". It is the precisely the nature that certain peptide can be developed into successful drug and other peptides cannot that indicate the high "unpredictability" of the art. The question is "predictability" of the art for various peptide drug, and it is NOT a question of whether peptides can or cannot be used as drugs. (see *In re Wands*, 8 USPQ2d 1400(1988)).

Applicants also argue that because the instant claims have no limitation or requirement for "oral delivery" of drugs, the Russell-Jones reference is irrelevant. Contrary to applicant's assertion, the instant claims are broad and encompassing various "pharmaceutical compositions" that can be delivered through different route. The instant specification does not specifically define the term "pharmaceutical composition" to exclude oral delivery. In fact, the instant specification contemplates oral delivery of the claimed "pharmaceutical composition" (Spec. p. 46, lines 15+). Nevertheless, the Russell-Jones reference demonstrates the high "unpredictability" of using peptide as pharmaceutical composition in the aspect of drug delivery (i.e. problems with administering to animals and/or human).

Applicants also argue that the instant invention does not have the "cell penetration" problem associated with peptide drugs that are discussed in the El-Andaloussi reference, because

the instant claimed ligand bind to "a cell membrane protein" (i.e. the ST receptor). However, the instant specification does not specifically define the ST receptor is "a cell membrane protein" (see Definition for "ST receptor" on p. 6 of the instant spec.). As discussed above, the instant claimed invention is broad and encompassing pharmaceutical compositions for treatment of various diseases. The only examples of "pharmaceutical composition" are the conjugates used to inhibit T84 cells in vitro in the instant specification at p. 72-75 (especially Example 6). The instant specification does not disclose any pharmaceutical composition other than the conjugates used to inhibit the T84 cells. It is not clear if the delivery to T84 cells can be "reasonably correlated" to delivery to other types of cells, or cells within an animal or human.

Thus, the previously cited references demonstrate "unpredictability" of various aspects of using peptide drugs. There are no predictable ways in the art to indicate which peptide drug can be successfully made and used in animals and human. The instant specification also does not provide guidance and/or examples to reasonably correlate the in vitro data (i.e. cell data) to in vivo usage (i.e. usage in human and animals). Thus, undue experimentation would be required to make and use the instant claimed invention in its full scope.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 42 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duflot et al (US 4,499,080; 2/12/1985; cited in the previous Office action 5/3/05), in view of Gluck et al (US 6,040,167; 3/21/2000; priority date 11/2/1992 or earlier). The previous rejection over claim 42 is maintained for the reasons of record as set forth in the Office action, mailed 9/6/06, at pp. 17+. The rejection over claim 57 is necessitated by applicant's amendment to the claims.

The secondary reference "Gluck" was inadvertently cited as Goers et al (US 4,867,973) in the previous Office action. However, as pointed out by applicants, the body of the previous rejection discussed the teaching of Gluck et al (see the recitation below). Thus, applicant's argument against the Goers reference is moot.

Duflot et al, throughout the patent, teach pharmaceutical compositions comprising conjugates of ST receptor binding moiety (i.e., see claims 1-34) and an agent (toxin) (i.e., see claims 21-34), which reads on the pharmaceutical composition of **clm 42**. The 2nd peptide in Claim 18 or the cytotoxin of Claim 31 of the reference would read on the "radiostable active agent" of **clm 42** because the instant specification defines the term "radiostable" as compounds which are not radioactive at p. 7, para 4. The reference also teaches buffers in which the said conjugates are contained for immunization (col. 15, lines 50+), and pharmaceutical compositions (e.g. Claim 33 of the reference), which reads on the pharmaceutical carrier or diluent of **clm 42**. The reference discloses ST receptor binding peptides comprising 18 amino acids of sequence Asn-Thr-Phe-Tyr-Cys-Cys-Glu-Leu-Cys-Cys-A-Pro-Ala-Cys-Ala-Gly-Cys-T, in which A and T each represent Tyr or Asn, and A and T are not the same (i.e., see Abstract or claim 1), which read on the SEQ ID Nos 2 and 3 of the instant claims.

The reference also teaches injecting the composition (e.g. col. 16, lines 3+ and 50+), which reads on the injectable pharmaceutical composition of **clm 57**.

Duflot et al do not specifically teach the pharmaceutical composition comprises a liposome.

However, Gluck et al, throughout the patent, teach a similar pharmaceutical composition comprising a liposome vesicle (part (a) of Claim 1 of the reference), a fusion peptide (part (b) of Claim 1), and a protein for binding receptor (part (d) of Claim 1). The reference teaches the benefits or advantages of using liposome vesicles to deliver particular drugs (col. 1, lines 55+). The advantages include facilitating transporting the drug through normally impermeable barriers, and improving drug selectivity and reduction in toxicity, etc. (col. 1, lines 57+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to using liposome vesicles to deliver various drugs.

A person of ordinary skill in the art would have been motivated at the time of the invention to use liposome as part of a pharmaceutical composition that comprise fusion peptides (or conjugates) with active drug agents, because using liposome vesicle to deliver drugs offer many advantages such as high permeability and low toxicity as discussed supra.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications because Gluck et al have demonstrated the utilization of liposome vesicle as part of a pharmaceutical composition that comprise peptides, and receptor binding proteins.

Discussion and Answer to Argument

13. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the Duflot reference teaches away from the instant invention (Reply, p. 18, para 2).

In support of applicant's "teaching away" assertion, applicants cited one of the "intended uses" of the recited product:

"Duflot et al. teaches to conjugate its synthetic peptides with a non-toxic carrier protein so that the sequences which induce antibodies that cross-react with ST are immunogenic. The non-toxic carrier is intended to assist in presenting the peptide sequences in immunogenic form. Examples of the non-toxic carrier protein provided in the specification include pathogen toxins. In suggesting the use of pathogen toxins, Duflot et al indicate that the benefit of such choices is that the non-toxic carrier protein serves as an additional immunogenic target. Thus, the use of cholera toxin sequences or Shigella toxin serves the duel purpose of 1) assisting in presentation of the ST peptide sequences in immunogenic form to induce an immune response that will cross-react with ST as well as 2) serving as an immune target itself for inducing an immune response against the pathogen from which the toxin sequences were derived."
(Reply, p. 18, para 3).

Applicant's above recitation of the reference's teaching (intended uses of the "cholera toxin") does not demonstrate that the toxin cannot be combined with a liposome. Nothing in the reference explicitly teaches that peptide cannot be combined with a liposome. Regardless of the intended uses of the reference's teaching, the Duflot reference teaches the claimed composition of ST peptides (or toxin).

As stated in the body of the rejection, "A person of ordinary skill in the art would have been motivated at the time of the invention to use liposome as part of a pharmaceutical composition that comprise fusion peptides (or conjugates) with active drug agents, because using

liposome vesicle to deliver drugs offer many advantages such as high permeability and low toxicity" as taught by the Gluck reference.

Applicants also seem to argue the above rejection by attacking the teaching of Duflot only. (Reply. pp. 18-19).

As discussed in the previous Office action, the rejection is based on the combination of the Duflot and the Gluck references. The Gluck reference provided explicit motivation to combine the references.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants also seem to argue that the Duflot reference does not teach the "radiostable active agent" of the present claim. (Reply, p. 18, para 3).

As discussed in the previous office action, the term "radiostable active agent" is broadly defined as therapeutic or imaging agents "which are not radioactive" (Spec. p. 7, paras 3-4). Thus, a compound that is not radioactive would read on the "radiostable active agent" according to the instant definition. As discussed in the previous office action, the 2nd peptide in Claim 18 or the cytotoxin of Claim 31 of the Duflot read on the "radiostable active agent", because the peptides are non-radioactive and can be used as imaging or therapeutic agents.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5,962,220

16. Claims 23, 25-28, 33, 34, 38, and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, and 6 of U.S. Patent No. 5,962,220 (cited in the previous Office action 5/3/05). Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claims the same pharmaceutical compositions as the instant application.

6,087,109

18. Claims 23, 25-28, 33, 34, 38, and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 7-10 and 13 of U.S. Patent No. 6,087,109 (Claims 5 and 1 of the '220 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claims the same pharmaceutical compositions as the instant application.

7,097,839

19. Claims 23 and 28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24, 26, 28, 29 and 33-41 of U.S. Patent No. 7,097,839. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claims the same pharmaceutical compositions as the instant application.

5,962,220 and 6,040,167

20. Claims 23, 25-28, 33, 34, 38, 40, 41, 42, 45, and 47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 6, 10, and 12 of U.S. Patent No. 5,962,220 in view of Gluck et al (US 6,040,167; 3/21/2000; priority date 11/2/1992 or earlier).

Discussion and Answer to Argument

21. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants state "applicant will file appropriate terminal disclaimers upon indication that the pending claims would be otherwise allowable" for the following patents:

5,962,220; 6,087,109; 7,097,839.

However, the instant claims have not been indicated as allowable, and applicants have not filed the appropriate terminal disclaims to overcome the above rejections. Thus, the said rejections are maintained for the reasons of record.

Applicants also assert that the combination of the '220 patent and the Gluck references (which was inadvertently cited as Goers in the preamble of the rejection in the previous Office action) do not render the present invention obvious. (Reply, pp. 19-20, bridging para).

However, applicants have made the above assertion without providing any reason or supporting arguments. Thus, the rejection is maintained for the reasons of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
5/7/07

JON EPPERSON
PRIMARY EXAMINER